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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/765,739	01/18/2001	Robert Lawton	00-1278	9509

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EXAMINER
FORD, VANESSA L

ART UNIT	PAPER NUMBER
1645	10

DATE MAILED: 04/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/765,739	LAWTON ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *1-23 and 25-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-34* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2&8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group III, claims 21-24 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-20 and 25-34 are withdrawn from further by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

2. Claims 22-24 are objected to because of the following informalities: *Ehrlichia* is the name of a genus and should be italicized.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. *This is a written description rejection.*

The specification broadly describes as a part of the invention polypeptides consisting of the polypeptides SEQ ID Nos: 1-7. The specification states that "variants in which amino acids of the polypeptides of the invention are substituted, deleted or

added in any combination are contemplated by the invention". The specification also states " that naturally occurring variants and non-naturally occurring variants are included in the invention and may be produced by mutagenesis techniques or by direct synthesis" (page 7). Applicant has broadly described the invention as embracing any substitution, insertion or deletion change of amino acids throughout the length of the polypeptide sequence. Variants SEQ ID Nos: 1-7 correspond to sequences from other species, mutated sequences, allelic variants, splice variants, sequences that have a variant degree of identity (similarity, homology), and so forth. None of these sequences meet the written description provision of 35 U.S.C. 112, first, paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOs:1-7, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptide regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes

v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Therefore, only SEQ ID NOs:1-7 but not the full breadth of the claim (or none of the sequences encompassed by the claim) meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

4. Claims 21-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-7 are directed to isolated polypeptides selected from the groups consisting of SEQ ID NOs: 1-7 and variants thereof.

The specification is enabling only for the polypeptides of SEQ ID NOs:1-7 as disclosed in the specification. The specification states that "variants in which amino acids of the polypeptides of the invention are substituted, deleted or added in any combination are contemplated by the invention". The specification also states " that naturally occurring variants and non-naturally occurring variants are included in the invention and may be produced by mutagenesis techniques or by direct synthesis"

(page 7). The specification teaches that there are many tolerable and conservative amino acid substitutions which can be made that are not critical to protein function (pages 7-9). There is no guidance provided as to which amino acids can be added, deleted or substituted and the polypeptide ~~would~~ still have retain its biological function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides broadly encompassed by the claims and the claims broadly encompass a significant number of inoperative species. Since the amino acid sequence of the polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar activity requires a knowledge with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expected intolerant to modification) and detailed knowledge of the ways in which the polypeptide's structure relates to function. However, the problem of the prediction of polypeptide structure from mere sequence data of a single polypeptide and in turn utilizing predicted structural determinations to ascertain functional aspects of the polypeptide and finally what changes can be tolerated with respect thereto is extremely complex and outside of the realm of routine experimentation.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen multiple substitutions or multiple modifications of other types and the positions within the polypeptide's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar activity are limited in

any polypeptide and the result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any toerance to modifications , e.g., multiple substitutions. The sequence of some polypeptides is highly conserved and one skilled in the art would not expect tolerance to any amino acid modification in such polypeptides.

Factors to be considered in determining whether undue experimentation is required, are set forth in In re Wands 8 USPQ2d 1400. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Applying the above test to the facts of record, it is determined that 1) no declaration under 37 C.F.R. 1.132 or other relevant evidence has been made of record establishing the amount of experimentation necessary, 2) insufficient direction or guidance is presented in the specification with respect to selecting other antigens having claimed functional features, 3) the relative skill of those in the art is commonly recognized as quite high (post-doctoral level). One of skill in the art would require guidance, in order to make or use polypeptides that are variants of SEQ ID NOs: 1-7 in a manner reasonable in correlation with the scope of the claims. Without proper guidance, the experimentation is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 21-24 are rejected under 35 U.S.C. 102(a) as anticipated by Waner et al *(J Vet Diagn Invest, 2000, 12:240-244).*

Claims 21-24 are drawn to a device containing one or more polypeptides selected from the group consisting of the polypeptides shown in SEQ ID Nos:1-7 and variants thereof.

Waner et al teach the use of a device (i.e. a clinic ELISA test kit). Waner et al teach that *Ehrlichia canis* IgG antibody titers of serum samples were determined by using a commercial ELISA test kit containing plastic combs sensitized with *E. canis* antigen. Waner et al teach that the sera to be tested was incubated with the comb (containing antigen dots). Waner et al teach that after washing away unbound antibodies the comb were allowed to react with goat anti-dog IgG alkaline phosphatase conjugate. Waner et al teach that bound antibodies were detected with a precipitating chromogen, 5-bromo-4chloro-3-indolyl phosphate and nitro-blue tetrazolium. The polypeptide sequence contained on the plastic comb (i.e. device) would be inherent in

pages 240-241

the teachings of the prior art. It is well known in the art to include instructions for using polypeptides for the identification of an *Ehrlichia* infection in a mammal in a diagnostic kit. The instructions for performing various immunoassays (i.e. western blot, reversible flow chromatographic binding assay, enzyme linked immunosorbent assay or indirect immunofluorescense assay) are well known in the art. The device of Waner, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's device with the device of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the device of the prior art does not possess the same material structural and functional characteristics of the claimed device). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

6. Claims 21-24 are rejected under 35 U.S.C. 102(b) as anticipated by Cadman et al *(Veterinary Record, 1994, 135, 362).*

Claims 21-24 are drawn to a device containing one or more polypeptides selected from the group consisting of the polypeptides shown in SEQ ID Nos:1-7 and variants thereof.

Cadman et al teach a device (i.e a cross dot blot apparatus), nitrocellulose paper was coated with *E. canis* antigen. Cadman et al teach that 0.7 μg of protein in TBS was used per dot. Cadman et al teach that test sera was incubated with the antigen (dots on

nitrocellulose paper). Cadman et al teach that the bound antibody was detected with peroxidase-labeled goat anti-dog IgG and 4-chloronaphthol. The polypeptide sequence contained on the nitrocellulose membrane (i.e. device) would be inherent in the teachings of the prior art. It is well known in the art to include instructions for using polypeptides for the identification of an *Ehrlichia* infection in a mammal in a diagnostic kit. The instructions for performing various immunoassays (i.e. western blot, reversible flow chromatographic binding assay, enzyme linked immunosorbent assay or indirect immunofluorescense assay) are well known in the art. The device of Cadman, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's device with the device of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the device of the prior art does not possess the same material structural and functional characteristics of the claimed device). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

7. Claims 21-24 are rejected under 35 U.S.C. 102(b) as anticipated by Zhi et al *(Journal of Clinical Microbiology, June 1998, p. 1666-1673).*

Claims 21-24 are drawn to a device containing one or more polypeptides selected from the group consisting of the polypeptides shown in SEQ ID Nos:1-7 and variants thereof.

Zhi et al teach a device (i.e dot blot apparatus comprising a nitrocellulose membrane). Zhi et al teach that the affinity-purified protein in TBS was blotted onto a nitrocellulose membrane and immersed in T-TBS containing 5% milk. Zhi et al teach that sera to be tested was diluted and incubated with the nitrocellulose membrane containing the dot of affinity-purified protein (i.e. polypeptide /antibody complex). Zhi et al teach that the affinity-purified protein was wash with T-TBS and incubated with peroxidase-conjugated affinity-purified anti-human IgG. Zhi et al further teach that the peroxidase-positive band were detected by immersing the nitrocellulose membrane in a developing solution indicating *Ehrlichia* infection (page 1668, 1st column). The polypeptide sequence contained on the nitrocellulose membrane (i.e. device) would be inherent in the teachings of the prior art. It is well known in the art to include instructions for using polypeptides for the identification of an *Ehrlichia* infection in a mammal in a diagnostic kit. The instructions for performing various immunoassays (i.e. western blot, reversible flow chromatographic binding assay, enzyme linked immunosorbent assay or indirect immunofluorescense assay) are well known in the art. The device of Zhi, et al appears to be the same as the claimed invention.

Since the Office does not have the facilities for examining and comparing applicant's device with the device of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e.,that the device of the prior art does not possess the same material structural and functional characteristics of the claimed device). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Pertinent Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure *(Unver et al, Journal of Clinical Microbiology, Dec 1999, p. 3888-3895 and McBride et al, Journal of Clinical Microbiology, January 2001, p. 315-322).*

Status of Claims

9. No claims are allowed.

Conclusion

10. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308–0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 308-4242.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (703) 308-4735. The examiner can normally be reached on Monday – Friday from 7:30 AM to 4:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (703) 308–3909.

Vanessa L. Ford
Biotechnology Patent Examiner
April 4, 2002

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